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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,782	10/17/2003	Harald W. Sontheimer	2006636-0064	7705

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
06/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/686,782	Applicant(s) SONTHEIMER ET AL.	
	Examiner Shin-Lin Chen	Art Unit 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 25 May 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *25 May 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1 and 15-28*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Shin-Lin Chen
Primary Examiner
Art Unit: 1632

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments from page 6-10 of the amendment filed 5-25-07 appears to aim at the utility of the claimed invention, which is irrelevant to the Official action mailed 11-21-06. The rejection in the Official action mailed 11-21-06 is 35 U.S.C. 112 first paragraph enablement rejection rather than a 35 U.S.C. 101 utility rejection. Even if the arguments are directed to the enablement rejection, they are not found persuasive because of the reasons of record. Applicants cite in re Brana and argue that several compounds within the scope of the claims exhibited significant antitumor activity against L1210 standard tumor model in vivo, and in the instant invention, there are in vitro evidence of specific binding of TM-601 (a form of chlorotoxin) to 18 different neuroectodermally derived tumors. Applicants asserted that chlorotoxin-derived molecules can be used to target specifically for therapeutic or diagnostic purposes of neuroectodermal tumors (amendment, 7-8). This is not found persuasive because of the reasons of record. The cited in re Brana is NOT analogous to the instant invention. The compounds in the in re Brana are themselves cytotoxic compounds that act on the tumor cells, however, the chlorotoxin itself is a carrier rather than a cytotoxic compound. chlorotoxin is used as a carrier to deliver the cytotoxic moiety to the targeted neuroectodermal tumors. It is the cytotoxic moiety that has the cytotoxic effect on the neuroectodermal tumors rather than the chlorotoxin itself. The claims read on using any cytotoxic moiety to treat numerous different neuroectodermal tumors. The phrase "cytotoxic moiety" is very broad that would encompass any protein or peptide or any molecule that is cytotoxic. Therefore, the claims encompass using proteins or peptides having unknown amino acid sequences and biological functions, and the biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention. Even the recited different toxins, antiviral proteins, and complement proteins have different amino acid sequences and different biological functions and whether they would able to treat different neuroectodermal tumors in vivo was unpredictable at the time of the invention. The dose of the cytotoxic moiety, the stability of said cytotoxic moiety during protein transfer in vivo, the amount of cytotoxic moiety at the target site, and the effect of the cytotoxic moiety on treating neuroectodermal tumor all vary among different cytotoxic moieties, however, the specification fails to provide such specific guidance for those various cytotoxic moieties recited in the claim. Thus, one skilled in the art would not know how to treat numerous neuroectodermal tumors in vivo by using various chlorotoxin-cytotoxic moiety complexes via various administration routes so as to provide therapeutic effect for treating said neuroectodermal tumor. Applicants cite Examples 21 and 23 of US Patent 5,905,027 and argue that chlorotoxin with radioactive moieties can be used to treat gliomas and chlorotoxin-GST fusion protein attached to the cytotoxic moiety saporin results in significant killing of the glioma cells (amendment, p. 8-9). This is not found persuasive because of the reasons of record and the reasons set forth above. Example 21 just provides a suggestion that chlorotoxin with radioactive molieties CAN BE used to treat gliomas. There is no evidence of record, in vitro or in vivo, that shows chlorotoxin with any dose of radiation can be used to treat glioma via various administration rotues. Example 23 only provide in vitro data, which cannot be extrapolated into success in vivo. Further, the chlorotoxin complex used in said example is different from what is claimed in the instant invention. Applicants cite declaration by Dr. Douglas Jacoby (In fact, it is Dr. Alison O'Neill's declaration) and argue that the I131-TM-601 can pass through blood-brain barrier to reach tumor in the brain and has therapeutic effect in vivo (amendment, p. 9-10). This is not found persuasive because of the reasons of record and the reasons set forth above. The declaration only discloses the survival rate of patient treated with 131I-TM-601 but fails to compare with control and it is unclear whether the survival of the patients is indeed due to the treatment of 131I-TM-601 via intracavitary or intravenous injection. Even if the survival of the patients treated with 131I-TM-601 is significantly higher than the control, only the particular dose of 131I-TM-601 with the particular administration route is enabled for treating glioma but NOT the full scope of the invention claimed. Applicants argue that chlorotoxin agent does pass through the blood brain barrier and Dr. Jacoby's declaration (it appears to be Dr. Alison O'Neill's declaration) confirms that TM-601 radiolabeled with iodine 131 does pass through the barrier to provide therapeutic effect (amendment, p. 11). This is not found persuasive because of the reasons of record and the reasons set forth above. Although iodine labeled chlorotoxin may pass through blood-brain barrier, however, the iodine labeled chlorotoxin is different from more complexed chlorotoxin-cytotoxic moiety, such as protein or nucleic acids. The larger size of cytotoxic moiety, such as protein, antibody and nucleic acid, may hinder the passing of the chlorotoxin complex through the blood-brain barrier. There is no evidence of record that shows other more complexed chlorotoxin-cytotoxic moiety can pass through the blood-brain barrier. Applicants argue that more than 18 examples of selective binding of TM-601 to different claimed neuroectodermally derived tumors and declaration confirms therapeutic effectiveness in humans (amendment, p. 11). This is not found persuasive because of the reasons of record and the reasons set forth above. Applicants argue that all of the cytotoxic moieties have a known biological function: they are cytotoxic, and the specification examplifies the effectiveness of at least two different cytotoxic moieties, 131I and saporin (amendment, p. 11). This is not found persuasive because of the reasons of record and the reasons set forth above. The term "cytotoxic" is a general term to describe a very general property of a group of molecules. For example, transporter proteins mean those proteins have function as a transporter, however, it does not mean they all transport the same compound or molecule. Each transporter protein could transport totally different compound or molecule, thus, they have different biological functions. Similarly, the claims encompass using proteins or peptides having unknown amino acid sequences and could have different biological functions, and the biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention. Even the recited different toxins, antiviral proteins, and complement proteins have different amino acid sequences and different biological functions and whether they would able to treat different neuroectodermal tumors in vivo was unpredictable at the time of the invention. The dose of the cytotoxic moiety, the stability of said cytotoxic moiety during protein transfer in vivo, the amount of cytotoxic moiety at the target site and the effect of the cytotoxic moiety on treating neuroectodermal tumor all vary among different cytotoxic moieties, however, the specification fails to provide such specific guidance for those various cytotoxic moieties recited in the claim. Thus, one skilled in the art would not know how to treat numerous neuroectodermal tumors in vivo by using various chlorotoxin-cytotoxic moiety complexes via various administration routes so as to provide therapeutic effect for treating said neuroectodermal tumor. Therefore, the claims are not enabled and remain rejected under 35 U.S.C. 112 first paragraph